

**NBCCEDP CERVICAL CANCER EXPERT PANEL**  
**WHITE PAPER ON TECHNOLOGIES**  
**FOR THE EARLY DETECTION OF CERVICAL NEOPLASIA**

**INTRODUCTION**

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The National Breast and Cervical Cancer Early Detection Program (NBCCEDP), administered by the Centers for Disease Control and Prevention (CDC) helps low-income, uninsured, and underserved women gain access to lifesaving screening services for the early detection of breast and cervical cancers. The NBCCEDP is implemented in all 50 states, 4 U.S. territories, the District of Columbia, and 13 American Indian/Alaska Native organizations. Through these grantees, the program implements a wide range of activities, including: (a) public education to raise awareness of the benefits of screening and the availability of subsidized screening services; (b) outreach to recruit high-risk women; (c) provision of breast and cervical cancer screening exams and diagnostic testing; (d) case management to facilitate access to care and assure completion of recommended follow-up testing; and (e) professional education and quality assurance to ensure the highest standard of care for women in the program. Although the program has screened 1.9 million women and provided 4.6 million screening examinations since it was established in 1991, it reaches fewer than 20 percent of eligible women annually, primarily due to limited Congressional appropriations.

Fiscal management of the multifaceted NBCCEDP poses many challenges; one in particular is the determination of which screening tests should be paid by the program. Appropriate stewardship of federal funds requires that decisions be evidence-based, yet there are market factors that influence the daily realities of the program. Since the program's inception, research and scientific advances have resulted in both changing recommendations regarding the timing and subjects of screening, but also the introduction of new technologies. Determinations about whether the NBCCEDP should pay for newer screening tests and procedures are complicated. The program must balance a wide range of factors, including, for example, standards of care for women in the program, the public health mandate to serve as many women as possible, limited program funds, varying local health services infrastructures, and the impact of changes in program policies on program operating procedures and partners.

Currently, the NBCCEDP provides screening reimbursement for conventional Papanicolaou (Pap) tests for screening and follow-up, and for human papillomavirus (HPV)/deoxyribonucleic acid (DNA) testing for women with atypical squamous cells of undetermined significance (ASC-US) findings on Pap. NBCCEDP policies do not support the use of federal funds for screening with liquid-based cytology (LBC) or combined cervical cytology screening and HPV DNA testing among asymptomatic women. These reimbursement policies are consistent with NBCCEDP screening policies and the most recent U.S. Preventive Services Task Force (USPSTF) evidence review for cervical cancer screening completed in 2003.

NBCCEDP screening policies were last reviewed in 1999 by CDC and an external working group. The resulting cervical cancer policies encouraged all NBCCEDP grantees to (a) focus cervical cancer screening on women who had rarely or never been screened, and (b) decrease

over-screening of women who had received numerous annual negative Pap tests in the program. CDC changed its screening policies and associated reimbursement policies from a recommended annual Pap test for all women to a Pap test every 3 years after a woman has had three consecutive normal Pap test results within a 5-year period. For women who have not had three consecutive Pap tests with normal or benign findings within a 5-year period, annual screening is still recommended. As shown in Table 1, NBCCEDP screening policies differ only slightly from the screening guidelines established by the American Cancer Society (ACS) and the American College of Obstetricians and Gynecologists (ACOG).

<b>Table 1: Cervical Cancer Screening Guidelines</b>			
	American Cancer Society <sup>1</sup> (ACS, Nov. 2002)	U. S. Preventive Services Task Force <sup>2</sup> (USPSTF, Jan. 2003)	American College of Obstetricians and Gynecologists <sup>3</sup> (ACOG, Aug. 2003)
<b>When to start</b>	Approximately 3 years after onset of vaginal intercourse, but no later than age 21	Within 3 years of onset of sexual activity or age 21, whichever comes first	Approximately 3 years after onset of sexual intercourse, but no later than age 21
<b>Intervals</b> <b>Conventional Pap test</b>	Annually; every 2-3 years for women $\geq 30$ with 3 negative cytology tests*	At least every 3 years	Annually; every 2-3 years for women $\geq 30$ with 3 negative cytology tests*
<b>If liquid-based cytology used</b>	Every 2 years; every 2-3 years for women $\geq 30$ with 3 negative cytology tests*	Insufficient evidence	Annually; every 2-3 years for women $\geq 30$ with 3 negative cytology tests*
<b>If HPV testing used</b>	Every 3 years if HPV negative, cytology negative	Insufficient evidence	Every 3 years if HPV negative, cytology negative
<b>When to stop</b>	Women $\geq 70$ years with $\geq 3$ recent, consecutive negative tests & no abnormal tests in prior 10 years*	Women $> 65$ years with negative tests, who are not otherwise at high risk for cervical cancer	Inconclusive evidence to establish upper age limit
<b>Post total hysterectomy</b>	Discontinue if for benign reasons & no prior history of high-grade CIN*	Discontinue if for benign reasons	Discontinue if for benign reasons & no prior history of high-grade CIN*

\*Some exceptions apply (e.g., women who are immunocompromised, have a history of prenatal exposure to DES, etc.). See guidelines for details.

In the context of feedback from several NBCCEDP programs about problems stemming from current reimbursement policies and small differences in screening guidelines, CDC initiated a review of its NBCCEDP cervical cancer reimbursement policies. Recognizing the complexity of the review task and the significant impact on individual programs, CDC initially sought to gather information about programs' experiences with reimbursement policies. Key informant interviews were conducted with NBCCEDP Program Directors representing eight state programs and with two CDC program staff to identify the range of issues that should be considered in CDC's evaluation of reimbursement policies. These interview findings are presented in Appendix A. Additionally, CDC identified key scientific references to provide general

background about current and newer technologies. The evidence overviews and discussions with experts demonstrated a lack of scientific evidence in many relevant areas, particularly regarding direct comparisons of test performance characteristics, such as sensitivity and specificity, and in utilization patterns among the technologies.

The complexity of program issues and paucity of directly relevant scientific evidence led CDC to implement a review process relying primarily on expert opinion to guide its decision-making about reimbursement policies. An expert panel was established including researchers, clinicians, public health practitioners and NBCCEDP Program Directors. A list of expert panel members is included in Appendix B. This expert panel was charged with: (a) identifying minimum criteria for establishing new reimbursement policies; (b) identifying a framework of issues to be considered in policy review; (c) providing specific recommendations for policy revisions for the reimbursement of LBC and combined cervical cytology screening with HPV DNA testing in asymptomatic women; and (d) providing guidance concerning procedures for future reviews of reimbursement policies.

Members of the expert panel on cervical cancer reimbursement policies conferred in subgroups and as a full committee through a series of conference calls and a face-to-face meeting held in Atlanta on April 14-15, 2005. This white paper provides the background for and final recommendations of this expert panel. The first two sections of this paper provide general information about the epidemiology of cervical cancer and screening for cervical cancer in the NBCCEDP. The next two sections provide context for assessing individual technologies by defining the minimum criteria that must be met in order to recommend reimbursement, and the range of specific test characteristics and public health factors that must be assessed in making reimbursement policy decisions. The final two sections review the test characteristics and public health factors for each technology under consideration and present the expert panel's recommendations. Recommendations are presented not only for reimbursement policies, but also for additional research and surveillance, patient and provider education, and the reimbursement policy review process.

## **CERVICAL CANCER**

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An estimated 10,370 women will learn they have cervical cancer, and 3,710 women will die from cervical cancer in the United States in 2005.<sup>4</sup> Nevertheless, U.S. cervical cancer mortality has decreased by more than 70 percent over the last 5 decades. Formerly the number-one cause of cancer deaths among U.S. women, cervical cancer ranked 14<sup>th</sup> in 2003.<sup>5</sup> These dramatic declines are in large part attributable to the widespread use of the Pap test to detect cervical abnormalities. Approximately half of the cervical cancers currently diagnosed in the United States are in women who have never received a Pap test, and an additional 10 percent of cancers occur in women who have not been screened within the past 5 years.<sup>6</sup> In developing countries, where utilization of Pap tests remains low, cervical cancer continues to be a leading cause of cancer-related death among women.<sup>7</sup>

Virtually all cervical cancer is caused by HPV, a sexually transmitted infection that includes more than 100 subtypes. More than 40 HPV types infect the genital tract; of these, about 15 are considered oncogenic or "cancer associated" types.<sup>7</sup> HPV 16 is the most common oncogenic

HPV type and is the type associated with the greatest attributable risk for cervical cancer. Most HPV infections are transient. Approximately 70 percent of high-risk HPV types regress within three years and over 90 percent of low-risk types regress within this same timeframe.<sup>1</sup> Progression from HPV infection to development of cervical cancer generally occurs over 10 or more years. HPV prevalence is highest among young women 20-24 years of age and declines until age 35 years. HPV prevalence remains stable from 35 years of age through 50 years of age, when it again decreases.<sup>8</sup> Women between the ages of 20 and 24 years have an HPV prevalence of 21 percent,<sup>8</sup> while women 35 years of age and older have an HPV prevalence in the range of 5 to 15 percent.<sup>9,10</sup>

Cervical cancer screening is based on cervical cytology, the microscopic analysis of cells gently scraped from the surface of the cervix and endocervical canal. Abnormal cell changes are most often reported using the Bethesda System.<sup>11</sup> This system categorizes squamous intraepithelial lesions as low-grade (LSIL) or high-grade (HSIL). Equivocal squamous changes are termed ASC-US or atypical squamous cells - cannot exclude HSIL (ASC-H). Because cervical cytology screening can identify precancerous lesions, invasive cervical cancer can actually be prevented. The primary focus of cervical cytology screening is detection of squamous lesions of the cervix. Cervical cytology may be less effective for detection of endocervical glandular lesions, possibly because of their less accessible location in the endocervical canal. For women who have undergone total hysterectomy with removal of the cervix, cervical cytology is not recommended unless the hysterectomy was performed because of cervical neoplasia or cancer or unless some cervical tissue remains post hysterectomy.

Conventional cervical cytology, however, has limitations, including recognized false-negative and false-positive rates. Further, abnormal cytologic findings do not always correlate with the ultimate severity of disease found on histologic examination of tissue. About 10 percent of ASC-US is found to be CIN3 on full evaluation.<sup>12</sup> For ASC-US that is HPV positive and for LSIL, approximately 15 percent will be found to be CIN3 on full evaluation.<sup>13</sup>

Current recommendations for women with abnormal cytologic findings of LSIL, HSIL, ASC-H or HPV-positive ASC-US call for follow-up by colposcopy-directed tissue biopsy in most cases. Special circumstances are noted for the management of LSIL among adolescents and post-menopausal women with LSIL, for whom repeat cytology and/or HPV DNA testing in a year are options.<sup>14</sup> Histologic examination of tissue is most commonly reported using CIN terminology with a grade 1-3 designation based on the proportional thickness of the epithelium displaying involvement of significant abnormal cells. CIN 1 is generally associated with transient HPV infections, and most such lesions regress over 6 months to 2 years. Current guidelines recommend treatment for most CIN 2 and 3. CIN 2 is used as the threshold for treatment for added safety, even though about one-third to one-half of CIN 2 would regress without treatment. CIN 3 does not usually regress. It is alternatively referred to as severe dysplasia/carcinoma in situ. CIN 3 and above (CIN 3+) is therefore a more rigorous endpoint for evaluating the effectiveness of a new technology and its impact on reducing cervical neoplasias and cancer.

## **SCREENING FOR CERVICAL CANCER IN THE NBCCEDP**

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The NBCCEDP serves age-eligible, low income, uninsured and underinsured women; this population represents about 10 percent of all women of screening age in the U.S. Current policy encourages all NBCCEDP grantees to focus cervical cancer screening primarily among women who have rarely or never been screened and to decrease over-screening of women already enrolled in the program. This approach is supported in part by evidence demonstrating that more than 60 percent of U.S. women who received a diagnosis of cervical carcinoma had never been screened or had not been screened within the previous 5 years of diagnosis.<sup>6</sup> Changes in NBCCEDP screening policies in 1999 established a screening interval for Pap testing every 3 years after a woman has had three consecutive normal Pap test results within a 5-year period.

In the case of cervical cancer screening, the NBCCEDP permits programs to screen women age 18 to 64 years of age. As with breast cancer, however, grantees set their own age criteria for cervical screening. From 1991 through 2002, more than half of the women receiving cervical cancer screening in the program were 40–59 years of age and 22 percent were under 40 years of age. Between 2001 and 2002, women under 40 years of age represented 17 percent of the total cervical cancer screening population. Racial and ethnic minorities represented 47 percent of the screened population between 1991 and 2002, a rate that increased slightly to 51 percent between 2001 and 2002.<sup>15</sup>

A 2001 Behavioral Risk Factor Surveillance System (BRFSS) report found that more than 90 percent of women 18 years of age or older with an intact cervix reported ever having a Pap test. These national rates were highest among older age groups and white non-Hispanic women.<sup>16</sup> A study of NBCCEDP women enrolled in the program between 1995 and 2001 found that 76 percent reported having previously received a Pap test before entering the program. The fact that this uninsured group reports screening rates lower than reported rates among the general population is not surprising.

For all women receiving cervical cancer screening for the first time through the NBCCEDP between 1991 and 2002, the percentage of abnormal screening results was 2.7 percent. The percentage of women with abnormal Pap test results was higher in the first screening round and among younger women. American Indian/Alaska Native women had the highest percentage of abnormal Pap test results; Asian/Native Hawaiian/Other Pacific Islander women had the lowest percentage.<sup>15</sup>

One study of NBCCEDP women receiving cervical screening between 1995 and 2001 also found that the proportion of either first or subsequent round abnormal Pap test results declined with increasing age. Similarly, all categories of CIN (1, 2, and 3) identified in either first or subsequent round screenings decreased with increasing age. The proportion of first round invasive cancers, however, increased with increasing age.<sup>17</sup>

From 1991 to 2002, rates of NBCCEDP biopsy confirmed CIN 2 or worse were 8.1 per 1,000 first round Pap tests and 2.6 for subsequent round tests. White women had the highest rates of first round CIN 2 or worse, followed by Hispanic/Latina women (7.1 and 5.7, respectively). Regardless of age, race, or ethnicity, detection rates were lower in subsequent compared to first rounds.<sup>15</sup>

The positive predictive value (PPV) of an abnormal Pap test in the NBCCEDP between 1991 and 2002, defined as the proportion of Pap test results of LSIL, ASC-H, HSIL, atypical glandular cells, and squamous cell cancer combined that led to a diagnosis of CIN 2 or worse, was 25.4 percent for first round Pap tests and 14.1 percent for subsequent round Pap tests. The PPV was highest for women in their 30's and white women.

A nationally representative study of providers conducted in 2004 found that of the clinicians providing Pap tests, about one third reported being part of the NBCCEDP. Approximately 75 percent of NBCCEDP participating clinicians reported using LBC while 60 percent reported ordering HPV DNA testing for borderline or abnormal cytology.<sup>18,19</sup> Rates of LBC use and HPV testing among NBCCEDP participating clinicians were similar to their specialties nationally, supporting the general impression that providers participating in the NBCCEDP are very typical of the universe of providers.<sup>19</sup>

## **REIMBURSEMENT DECISION CRITERIA**

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Review of NBCCEDP reimbursement for new screening technologies must consider the overall advantages and disadvantages of the new technology relative to the mission of the NBCCEDP and current screening approaches. Because screening is performed on healthy, asymptomatic women, each new technology must clearly demonstrate its ability to perform equally or better than current technologies. Overall, the technology must meet certain minimum criteria. These include:

- Reduce Cervical Cancer Morbidity and Mortality – The technology must contribute to reductions in morbidity and mortality across the population of program eligible women. For cervical cancer screening, reductions in morbidity and mortality come from identifying and treating precancerous lesions and preventing invasive disease by removing cervical neoplasia.
- Sustain or Enhance Overall Public Health Benefit – Use of the technology should sustain or enhance the number of program eligible women served by the NBCCEDP, for example, by maintaining or increasing access to services or maintaining or increasing dollars available to pay for services.
- Sustain or Enhance Overall Quality of Care – Use of the technology should sustain or enhance the quality of services provided by the NBCCEDP, for example by enhancing effectiveness, reducing false-positive findings, or improving test acceptability and patient adherence.
- Sustain or Enhance Overall Program Operations – Use of the technology should sustain or enhance program operations across NBCCEDP sites, for example by streamlining administrative procedures, maintaining or increasing provider enrollment, or enhancing clinical efficiency.
- Reduce Overall Health Disparities – Use of the technology should further NBCCEDP goals to reduce disparities in the delivery of services to and health outcomes of low-income, uninsured, and underserved women.

Beyond these minimum criteria for establishing reimbursement policies, consideration must be given to two additional factors. First, policies must accommodate differences across programs. NBCCEDP programs differ considerably in public health infrastructures as well as local health care capacities and systems. Reimbursement policies must be consistent across programs while still affording flexibility in how NBCCEDP programs implement these policies across local communities.

Second, as a federal government agency, the CDC must consider related policies established by other federal agencies, in particular the Food and Drug Administration (FDA) and the Centers for Medicare and Medicaid Services (CMS). Each federal agency establishes policies consistent with its unique mission. Unlike the CDC, FDA and CMS are regulatory agencies. The FDA provides market approval for new drugs and devices, and CMS provides payment approval and establishes reimbursement rates for the delivery of medical services under mandated federal entitlement programs. The NBCCEDP relies on the rate structure established by CMS for reimbursement of early detection and diagnostic services in Medicare and it is statutorily mandated that NBCCEDP reimbursement not exceed Medicare rates.

Reflective of the different missions of these agencies, the procedures each uses to establish policies also differ. FDA seeks to establish whether a medical drug or device is safe and as effective as existing technologies, and the agency relies in part on input from industry and industry-sponsored studies in making these determinations.<sup>20</sup> CMS seeks to identify medical procedures for reimbursement under Medicare and Medicaid. Its determinations are based on whether a procedure, device, or technology is “reasonable and necessary” for the diagnosis and treatment of a medical condition.<sup>21</sup> Like the FDA, CMS also invites industry collaboration and comment during its approval process. Importantly, however, neither CMS nor FDA approval of a new procedure, drug, device or technology indicates that it is *more* effective than existing procedures, drugs, devices, or technologies.

Some components of these approval procedures overlap across federal agencies. For example, CMS requires that drugs or devices be approved as safe and effective by the FDA before it will provide approval for reimbursement under Medicare or Medicaid. But it is also true that some components remain independent. For example, CMS provides approval for some procedures (e.g., preventive services counseling), that do not fall within the authority of FDA’s mandate to establish safety and efficacy because it is not a drug or device.

Establishment of reimbursement policies under CDC’s NBCCEDP must first reflect the unique mission of the program: maximizing reductions in cervical cancer morbidity and mortality in the eligible population of low-income, uninsured women. Procedures for establishing these policies rely primarily on scientific evidence, expert opinion, and program considerations. In this context, it is not surprising that CDC policies in some cases will overlap with those of the FDA and CMS, while in others they may not. For example, while CDC might require that all reimbursed technologies be approved by FDA as safe and effective for the same use, there may be program services for which FDA has no authority (e.g., preventive services counseling). Similarly, there may be circumstances where CMS has approved a technology or procedure and established associated reimbursement rates, but

the benefits of the technology for the NBCCEDP are outweighed by disadvantages such as high costs, overall cost effectiveness, lack of clinical availability, or program inefficiencies.

For these reasons, absolute requirements for FDA and/or CMS approval for all NBCCEDP reimbursed technologies were considered overly restrictive. Further, any requirement that the NBCCEDP reimburse for all FDA and/or CMS approved technologies was considered inappropriate as this might result in limiting the program's ability to achieve its mission to extend services to as many eligible women as possible in order to maximize reductions in breast cancer morbidity and mortality. Thus, it is recommended that:

- for all technologies and procedures within FDA authority, the technology should be approved by the FDA for the use under consideration, and
- for all technologies and procedures within CMS authority, the technology should be approved by CMS and Medicare rates established, but not all CMS approved technologies need to be reimbursed by the NBCCEDP.

## **BASIS FOR TECHNOLOGIES ASSESSMENT**

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The basis for decisions about whether the NBCCEDP should provide reimbursement for any new technology combines a full range of test characteristics and program factors. This section presents an overview of the components of this assessment. Table 2 lists and provide definitions for each test characteristic considered and Table 4 lists and provides definitions for each public health factor considered.

### ***1. Test Performance Characteristics***

- Sample Adequacy – Sample adequacy reflects the sufficiency of a sample for accurate interpretation. Adequacy is affected by sample collection characteristics as well as the quality of the sample for interpretation. The type of collection instrument, the person collecting and handling the sample, as well as characteristics of the woman being sampled (e.g., age, menstruation, inflammation) may all affect the quality of the sample. Sample quality is reduced by the inclusion of materials in the sample that obscure cells or the absence or insufficient numbers of cells from the transformation zone.

Sample adequacy can influence the sensitivity of a test. A sample that is less than optimal may be more likely to be reported as negative if abnormal cells are missing or if interpretation is hampered by obscuring factors, such as mucous and blood.<sup>22,23,24</sup> When a sample is inadequate for interpretation, a woman must return for a repeat test which increases the costs associated with using the test. One common measure reflecting poor sample adequacy is the proportion of samples categorized as unsatisfactory for interpretation.

Although large systematic reviews of sample quality have been published in the last several years, data are sparse and contradictory. In general, current evidence about sample adequacy across cervical screening technologies is insufficient for comparisons.



- Sensitivity – Test sensitivity reflects the ability of a test to detect high-grade dysplasia and cervical cancers when they are present. All other things being equal, a more sensitive test should lead to greater detection of CIN, the treatment of which leads to reduced incidence, morbidity, and mortality. However, the natural history of cervical neoplasia is unique. Because most cases of CIN 1 and potentially “true” CIN 2 will resolve spontaneously without progression to cancer, greater test sensitivity will detect more transient, clinically insignificant disease. Because transient lesions are much more common than lesions that will become cancer, the overall decreased costs associated with early treatment of lesions that would have progressed to cancer are offset by large increased costs associated with managing transient lesions. The magnitude of increased costs associated with the management of transient lesions is further influenced by the threshold used for a positive test finding. When a lower threshold for disease is used, such as CIN 1, the number of transient, clinically insignificant lesions identified will be even larger than when CIN 2 or 3 is used, resulting in even larger overall increases in screening costs.<sup>25</sup>
- Specificity – Test specificity reflects the ability of a test to accurately identify individuals without disease. Lower test specificity increases false positive findings which lead to unnecessary procedures, costs, and anxiety for women. For any single test, specificity generally decreases as sensitivity increases.

In a screening context, because the prevalence of clinically significant cervical abnormalities is very low, increases in sensitivity result in small reductions in missed abnormalities. But even small decreases in specificity can result in large increases in the number of false positive findings. For example, in a population of 100,000 women for which a true prevalence of clinically significant cervical abnormalities is 1 percent, 99,000 women would be normal (99 percent) and 1,000 would have cancer. A test having a sensitivity of 80 percent would find 800 abnormalities, but would miss 200 abnormalities. An increase in test sensitivity of 10 percent, to a sensitivity of 90 percent, would result in half as many missed abnormalities, or 100 fewer missed clinically significant abnormalities. But more dramatically, even smaller decreases in specificity result in a substantially larger number of women receiving a false positive test result. If test specificity is 90 percent, 10 percent of the 99,000 women, or 9,900 women would incorrectly receive a positive test result. A 5 percent absolute decrease in specificity to 85 percent translates into an additional 4,950 women receiving a false-positive test result. Decreases in test specificity which often accompany improvements in sensitivity can yield substantial increases in adverse patient consequences and costs associated with unnecessary follow-up tests. In the example given, an additional detection of 100 clinically significant cervical abnormalities came at a cost of additional work up of 4,950 normal women. Differences in specificity between tests translate into differences in false-positive test results, thereby either increasing or decreasing the efficiency of detecting true CIN 2+. One measure reflecting the efficiency of a test is the percent women referred for follow-up. This measure is based on both the true- and false-positive test results in the screened population and avoids the need to define a negative test

result. Studies that have assessed sensitivity and specificity using longitudinal data show that misclassification of disease is in fact a concern, especially for histology results of CIN 1 and CIN 2 because these may progress or regress between consecutive screenings.<sup>26</sup>

**Table 2: Definitions of Test Characteristics for Assessing Reimbursement Policies for Cervical Cancer Screening Technologies**

<b>Test Characteristic</b>	<b>Definition</b>
<b>Test Performance</b>	
Sample Adequacy	The sufficiency of a sample for accurate interpretation. Adequacy is influenced by sample collection characteristics as well as systems for assessing and establishing minimum sample quality. One indicator of poor sample adequacy is the percent of samples that are unsatisfactory, thus requiring repeat collection.
Sensitivity	The proportion of individuals who have the disease in a tested population for whom the test results from a satisfactory sample are positive.
Specificity	The proportion of all individuals who do not have the disease in the tested population for whom test results from a satisfactory sample, are negative.
Reliability of Interpretation	The extent to which the same exam result is obtained by different examiners interpreting the same sample.
<b>Test Frequency</b>	
Interval	The recommended time to repeat a test following a normal test.
<b>Test Costs</b>	
Test Reimbursement Rates	Current Medicare reimbursement rates for laboratory costs.
Repeat Medical Procedures/ Appointments	Proportion of repeat tests due to sample inadequacy, other processing errors, or ambiguous findings.

- Reliability of Interpretation – A key characteristic of any test used in widespread screening is reliability or the reproducibility of interpretation across raters (inter-rater) and by the same rater (intra-rater). Reliability of interpretation is most often measured by Cohen's Kappa, a measure of association used to assess inter- and intra-rater agreement on diagnostic tests. This measure takes into account the expected rate of agreement based on chance alone. As Cohen's Kappa increases, the strength agreement increases. If the results of a test vary based on who interprets the test or when the same individual interprets a test, test performance characteristics, such as sensitivity and specificity will vary widely. As discussed above, this can have important effects on the number of false-positive and false-negative findings. Further, this limits the ability to reliably assess cost-effectiveness across settings and develop cost-effective public health implementation strategies.

## 2. Test Frequency

- Interval – Interval refers to the time between screening tests following a normal test. More frequent screening generally costs more because more tests are performed. Because the majority of cervical cancers are slow-growing, frequent (annual) screening can compensate for decreased test sensitivity because it affords multiple opportunities to detect CIN before progression to cancer. On the other hand, because most CIN is transient, frequent screening will detect more clinically insignificant lesions that will never become cancer. As noted above, this causes unnecessary procedures and associated increased costs as well as increased anxiety and inconvenience for women. Further, negative health effects can result with no reduction in cancer morbidity or mortality. As screening becomes more frequent, costs rise at a substantially higher rate than effectiveness as reflected in reductions in cancer incidence and mortality.<sup>25,27,28,29,30,25, 31, 32</sup>

## 3. Test Costs

- Test Reimbursement Rates – The NBCCEDP reimbursement for covered procedures is based on current Medicare reimbursement rates set by CMS. As shown in Table 3, these rates vary across technologies. These Medicare test reimbursement rates reflect lab and test costs and do not include provider fees. Provider reimbursements are not necessarily constant across technologies because the time to perform a procedure or to counsel patients about test interpretation can vary. Generally, new technologies cost more initially on a per-test basis than existing technologies, although costs of new technologies tend to decline as adoption of the technology rises. The primary cost consideration when comparing different tests is the incremental difference between costs of the new test and the test that is currently in use. New technologies generally increase costs.

Table 3: 2005 Medicare Reimbursement Rates <sup>33</sup>					
CPT Code	Procedure	Low	High	Average	Median
88164	Pap Test, Conventional*	--	--	\$14.76	--
88142	Liquid-Based Pap Test	\$14.76	\$28.31	\$26.78	\$28.31
87621	HPV DNA Test**	\$27.41	\$49.04	\$46.52	\$49.04
*Conventional Pap tests are reimbursed at a single national rate.					
**HPV DNA testing is performed as an adjunct to cervical cytology and thus reflects an added, not a replacement cost.					

- Repeat Medical Procedures/Appointments – The need to repeat testing is a function of the adequacy of the sample and the strategy that is implemented for ASC-US test results. As mentioned previously, an unsatisfactory test will require collection of a new sample and a repeat medical visit. Some follow-up is required for ASC-US and LSIL, and clinicians may select different strategies for managing this situation. Strategies that result in a larger number of second visits can increase the overall cost of screening. Second visit costs include more than the medical costs of the test. They result in lost productivity for providers who cannot use that appointment time for another patient; for NBCCEDP program staff who provide case management and handle billing; and lost productivity and

inconvenience for patients who may need to take time from work and pay for transportation and/or child care.

Additional medical visits also can be associated with follow-up testing. In this context, reflex testing that relies on the use of an existing sample to perform follow-up tests based on the results of the initial test can considerably enhance clinical efficiency by avoiding the need for repeat medical visits. Providers do not have to collect a new sample and use additional clinic time, medical staff do not have to catalogue and process a new sample and patients do not have to return for a second visit.

<b>Table 4: Definitions of Public Health Factors for Assessing Reimbursement Policies for Cervical Cancer Screening Technologies</b>	
<b>Public Health Factor</b>	<b>Definition</b>
<b>Clinical Factors</b>	
Practice Patterns	Current and projected levels of utilization of a technology in medical practice, and regional variability in practice.
Clinical Efficiency	Impact of the use of a technology on the resources used per case.
<b>Patient Factors</b>	
Age	Influence of patient age at screening on test efficacy.
Acceptability/Adherence	The influence of test characteristics on patient acceptance of a test and its consequences. Acceptability is a major determinant in patient adherence to recommended testing intervals.
<b>Programmatic Factors</b>	
Programmatic Efficiency	Impact of the use of a technology on program resources – e.g., how it affects the complexity of billing procedures, staff time needed to bring women back into the system, and demands for provider and patient education.
Provider Enrollment	Impact of the use of a technology on the number of providers enrolled in programs.
Continuity of Care	The potential of the use of a technology to facilitate delivery of related health care services.

#### **4. Clinical Factors**

- Practice Patterns – Historically, the use of different medical technologies has varied at the individual provider level and across different geographic regions. Factors influencing adoption of new technologies include perceived strengths and weaknesses of the technology, industry marketing, patient demand, reimbursement rates, and potential efficiencies introduced by a new technology. As a result, some new technologies may be used almost exclusively in some areas served by the NBCCEDP, but not in others. This applies both to new and existing

technologies. For example, in areas where LBC has been widely adopted, use of conventional cytology may be very low. In other areas, providers may continue to rely primarily on conventional cytology. In areas where the new technology is in widespread use, failure to reimburse for a new technology or reimbursement rates based on established, lower-cost technologies can adversely influence provider enrollment and access to screening services. Further, as highlighted in key informant interviews, perceptions of program credibility can be adversely affected when the program does not reimburse for a technology that is in predominant use in an area and reimbursed by other insurers.

- Clinical Efficiency – Clinical efficiency refers to the extent of clinical resources, including both personnel and materials, required to deliver screening services. In general, use of the same screening test and/or procedures for all patients is more efficient than use of different tests for different patients. Different tests require staff time to determine which test is appropriate for which patients and may involve different procedures for sample collection and/or storage, requisitions, laboratories, or shipping. Use of different procedures associated with different tests also can introduce opportunities for medical errors.

Clinical efficiency also can be influenced by the sequence and/or timing of testing. Different clinical algorithms or numbers of visits within a specified timeframe for screening may be associated with different provider and staff time requirements. Reflex HPV DNA testing for ASC-US can considerably enhance clinical efficiency by avoiding the need for additional medical visits. Screening tests involving longer test intervals to achieve the same disease outcomes also can enhance clinical efficiency by reducing overall screening costs.

## 5. *Patient Factors*

- Age – Because of the natural history of cervical cancer, the transience of most HPV infections, and differences in CIN and HPV prevalence by age, the appropriateness of different screening tests varies by patient age. Half of all women diagnosed with cervical cancer are between 35 and 55 years of age. Further, because of prior screening and treatment opportunities, the prevalence of disease among previously screened women decreases with age<sup>34</sup>, thereby increasing the cost of screening within a given screening cycle with increasing patient age. Finally, the clinical significance of diagnoses may vary by age. Histologic CIN 2 may represent “exuberant” expression of CIN 1, not early “high grade” lesion in younger women.
- Acceptability/Adherence – Patients’ acceptance of a cervical cancer test and its consequences can influence adherence with screening, follow-up, and treatment recommendations. Factors influencing acceptance include for example, methods of sample collection, frequency of testing, repeat testing rates, false positive rates, and complexity of decision-making associated with test results. These factors can result in considerable burden for patients, thereby making the ‘cost’ of screening too high relative to the perceived benefits. For example, repeat office visits may require time off from work, day care fees, and transportation costs. False positive

findings may require unnecessary follow-up tests, anxiety and difficult medical decisions. Although newer cervical cancer technologies have been developed with improved sensitivity, implications for adherence have not been well addressed.

## 6. *Program Factors*

- Programmatic Efficiency – Program efficiency refers to the extent of NBCCEDP resources, including both personnel and materials, required to deliver screening services. Similar to clinical efficiency, use of the same test and/or procedures for delivering screening is generally more efficient than use of different tests for different patients. Different tests and combinations of tests can require different levels of staff time for case management, billing and financial management, and program monitoring. Little data are available about the impact of different testing scenarios on program costs.
- Provider Enrollment – Providers are critical to the NBCCEDP’s ability to deliver screening services. Reimbursement policies can in some circumstances create disincentives for provider participation which in turn could in some circumstances lead to decreased provider enrollment. Although generally infrequent, key informant interviews did note cases where providers withdrew from the program because of a large difference between their costs to delivery services and the level of reimbursement for a test.
- Continuity of Care – Establishing a long-standing relationship and regular visits to a provider are important components of ensuring integration and coordination across the medical care a woman receives. Limiting the universe of providers where women can be referred for cytologic screening can limit the ability of NBCCEDP women to continue seeing providers with whom they may have a long-standing relationship.

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## TECHNOLOGIES OVERVIEW

Three technologies for the early detection of cervical neoplasia are reviewed for screening reimbursement by the NBCCEDP, including conventional cytology, LBC, and HPV testing as an adjunct to cervical cytology. Each of these technologies is currently approved by the FDA. Other technologies, such as self-sampling (self-collected vaginal specimens for HPV DNA testing), likely will undergo FDA review in the next several years, but are not included in this review.

This section reviews test characteristics and public health factors associated with conventional cytology, LBC, and HPV testing. These issues combine uniquely for each technology. For example, some new technologies bring more favorable test characteristics, but at a test or program cost that on balance does not support the overall public health goals of the NBCCEDP. Other new technologies might bring only comparable test performance characteristics, but add program efficiencies or reduce test costs that potentially allow more women to be screened by the program. The unique combination of test characteristics and

public health factors will provide the basis for reimbursement policies recommendations presented in the following section.

An extensive systematic literature review of two of the three technologies being considered here, conventional cytology and LBC, was recently conducted for the USPSTF.<sup>35</sup> For these technologies they concluded: “Overall, the quality of this literature is poor for the purposes of making decisions about choice of screening systems in U.S. populations. No randomized trials or prospective cohort studies relate use of a screening modality over time to outcomes for individual women. The cost-effectiveness of use of new technologies has only been estimated, not measured directly. The most sophisticated and thorough cost model to date is significantly hindered by the limitations of the literature. Nonetheless, it demonstrates that, at present, new technologies are more costly than conventional cytology; only if used in screening intervals of 3 years or longer will new technologies fall within the traditional range considered to be cost-effective (\$50,000 per life-year).”

### **Conventional Cytology**

Conventional cytology includes the collection of a sample of cervical cells, transfer of these cells to a dry glass slide, preservation with a fixative, usually a spray, and interpretation of cytologic characteristics.

#### ***1. Test Performance Characteristics***

- **Sample Adequacy** – Cytologic samples are collected at the time of pelvic examination after visualization of the cervix. Samples are collected from the ectocervix using a spatula and from the endocervix using a brush or broom. These collection devices are made of special materials designed to collect and release cells. The combination of an ectocervical spatula with an endocervical brush is optimal.<sup>36</sup> No appreciable differences in sample adequacy were found in some studies comparing collection of endocervical cells using a brush or swab,<sup>37</sup> however, several other studies have found the swab to be significantly inferior to the brush at collecting endocervical cells.<sup>38,39,40,41</sup> Failure to collect or dislodge sufficient cells results in insufficient cellularity and contributes to unsatisfactory sampling.<sup>42</sup> Failure to rapidly and/or adequately fix a sample slide or over-vigorous fixing cells on a slide, results in unsatisfactory samples. The Bethesda 2001 classification system includes semi-quantitative criteria for assessing the quality of conventional cytology samples.

Traditionally, women are asked to avoid scheduling conventional cytology exams during menses, though the ACS guidelines state that cytology should be performed opportunistically if a return appointment is difficult. Blood and inflammation can obscure cells and result in unsatisfactory samples. Postmenopausal atrophy and the receding transition zone also contribute to difficulties obtaining an adequate sample.

- **Sensitivity** – Defining cervical disease as CIN 1 for histology and abnormal conventional cervical cytology as ASC-US or worse, the sensitivity of a single conventional cytology test is between 30 and 87 percent<sup>43</sup> The variation reflects difficulties in study design that can affect accuracy of disease ascertainment.

- Specificity – Defining cervical disease as CIN 1 for histology and an abnormal conventional cervical cytology as ASC-US or worse, the specificity of a single conventional cytology test is between 86 and 100 percent.<sup>43</sup>
- Reliability of Interpretation – Tabbara<sup>44</sup> reported a Cohen’s Kappa of 0.62 for interpretation of abnormal cases, reflecting 62 percent agreement across raters. Data from the College of American Pathologists Inter-Laboratory Comparison Program for cases that had been reviewed by at least five observers showed that the percentage of slides in which reviewer interpretations matched the reference interpretation varied between 8 and 73 percent, depending on the reference interpretation of the case.<sup>45</sup>

## **2. Test Frequency**

- Interval – The initiation of testing with conventional cytology is recommended within 3 years of onset of sexual activity or age 21, whichever comes first. Conventional cytology testing is recommended at least every 3 years thereafter until a woman is older than age 65 (USPSTF) or 70 (ACS) with a negative test history and not otherwise at risk (see Table 1). More frequent screening intervals are recommended by some groups for immunocompromised women.

## **3. Test Costs**

- Test Reimbursement Rates – The Medicare reimbursement rate for conventional cytology is \$14.76. This cost does not include provider fees.
- Repeat Medical Procedures/Appointments – Approximately 7 percent of conventional cytology tests require repeat testing due to ambiguous findings (ASC-US) or unsatisfactory samples.<sup>46</sup> Testing for high-risk HPV DNA cannot be performed on a conventional cytology sample. HPV follow-up to ASC-US findings requires either an additional sample at the time of conventional cytology or a repeat office visit for a second sample collection. If an additional sample is taken at the time of initial cytology, further clinical and laboratories procedures are required for storage and retrieval of samples as necessary.

## **4. Clinical Factors**

- Practice Patterns – Evidence suggests that most providers, more than three-quarters of those providing Pap tests, now use LBC,<sup>18</sup> and similar levels of LBC use appear among NBCCEDP participating clinicians.<sup>19</sup> As clinicians integrate LBC technology into their practices, many no longer keep supplies necessary for conventional cytology and proficiency levels in slide preparation, fixation, and interpretation may decline with infrequent application.
- Clinical Efficiency – Because the NBCCEDP currently reimburses only at the conventional cytology rate, NBCCEDP providers who routinely use LBC for their patients must either absorb the cost difference between conventional cytology and LBC or maintain supplies and systems for delivering both tests, LBC for non-program women and conventional cytology for NBCCEDP women. While it is



unclear how often practices adopt this latter approach, key informant interviews suggested that some practices may use a two-test approach at least during some transition phase. Maintaining two systems can greatly reduce clinical efficiency and may introduce opportunities for medical errors by introducing the need for procedures to identify NBCCEDP patients, procedures for maintaining different sets of supplies for different tests, and different procedures for laboratory processing and interpretation. In practice, providers are rarely aware of which patients are enrolled in the NBCCEDP and which are not.

## 5. *Patient Factors*

- Age – Conventional cytology is appropriate for women 3 years after the initiation of sexual intercourse or by age 21, whichever occurs first. The NBCCEDP currently screens women beginning at age 18.
- Acceptability/Adherence – Conventional cytology is familiar to most women. More than 90 percent of women 18 years of age or older in the U.S. with an intact cervix report ever having a Pap test.<sup>16</sup>

## 6. *Program Factors*

- Program Efficiency – Cervical cancer screening using conventional cytology has been an integral part of medical practice for many decades and most procedures and practices associated with the test are standardized and well established. Many of the clinical efficiencies stemming from this integration and standardization also extend to NBCCEDP operations and systems, allowing the program to extend cervical cancer screening services to larger numbers of women within its limited budget. However, as newer technologies supplant conventional cytology, program processes for supporting the older technology become increasingly fragmented, time consuming, and vulnerable to errors. Conventional cytology may result in higher overall program costs due to additional office visits for follow-up HPV DNA or cytology testing for ASC-US interpretations and program requirements resolving billing errors associated with different testing procedures for women in the program, in case management time associated with scheduling additional follow-up visits, and in staff discussion with providers and their staff about NBCCEDP reimbursement policies. Although no studies have directly compared the associated costs of conventional and LBC cytology and the impact of different test specificities, anecdotal program evidence from key informant interviews and rates of adoption of LBC suggest that the lower per-test cost of conventional cytology may increasingly be outweighed by these other costs.
- Provider Enrollment – As clinical practice patterns shift to use of LBC, providers increasingly report difficulty finding pathology laboratories that accept conventional cytology tests for interpretation. Further, providers that have adopted use of LBC for their practices find it increasingly difficult to maintain two approaches to cervical cancer screening, one for NBCCEDP patients and one for other patients. Many providers do not attempt to sustain two-test practices and absorb the cost difference associated with providing LBC to NBCCEDP patients. While absorbing the cost difference simplifies their office protocols, the

program's dependence on altruism is precarious and can adversely affect provider recruitment, particularly as this extends over time.

- Continuity of Care – The primary provider of care for many women is the provider from whom they receive their cervical screening examination. As practice patterns shift away from conventional cytology, it is possible that women will not be able to maintain long-term relationships with providers who no longer provide conventional cytology and are not members of the NBCCEDP.

### **Liquid-Based Cytology (LBC)**

Liquid-based cytology (LBC) includes the collection of a sample of cervical cells, transfer of these cells to liquid medium, and interpretation of cytologic characteristics.

#### ***1. Performance Characteristics***

- Sample Collection – Similar to conventional cytology, LBC samples are collected at the time of pelvic examination after visualization of the cervix. Samples are collected from the ectocervix using a spatula and endocervix using a brush or broom. These collection devices are made of special materials designed to collect and release cells. The combination of an ectocervical spatula with an endocervical brush is optimal.<sup>36</sup> No appreciable differences in sample adequacy were found in studies comparing collection of endocervical cells using a brush or broom.<sup>37</sup>

Unlike the preparation procedures for conventional cytology samples, the spatula and brush or broom are placed directly into a liquid media and vigorously agitated to release cells. Preservation is simplified and less dependent on operator technique than with conventional cytology. Inadequate samples result from insufficient cellularity, which in the case of LBC occurs due to poor sampling technique or failure to adequately release cells. Inadequate samples due to blood, inflammation, or atrophy occur with frequencies similar to conventional cytology tests. The Bethesda 2001 classification system includes more quantitative criteria for sample quality of LBC samples than of conventional cytology samples.

- Sensitivity – Defining cervical disease as CIN 2+ and an abnormal Pap test as ASC-US or worse, the sensitivities of a single LBC test of 61 percent<sup>9</sup> and 95 percent<sup>47</sup> have been reported.
- Specificity – Defining cervical disease as CIN 2+ and an abnormal Pap test as ASC-US or worse, the specificities of a single LBC test of 78 percent<sup>47</sup> and 82 percent<sup>9</sup> have been reported
- Reliability of Interpretation – Stoler<sup>26</sup> reported a Cohen's Kappa of 0.46 comparing interpretations rendered by two observers, reflecting 46 percent agreement. Data from the College of American Pathologists Inter-Laboratory Comparison Program compared larger numbers of observers and found that LBC generally showed less inter-observer variability than conventional preparations. However, the level of inter-observer variability differs somewhat with the reference interpretation, and certain subsets of HSIL and squamous carcinomas

actually show greater inter-observer variability than do the corresponding conventional tests.<sup>48</sup>

Proficiency and associated reliability of interpretation is influenced by the frequency of interpretation. Thus, reliability of interpretation for conventional cytology may be changing among providers who use LBC. Adoption of LBC appears to be high with one national survey finding that 77 percent of clinicians who reported providing cervical cytology used LBC.<sup>18</sup> Further, rates of HPV testing and use of LBC among NBCCEDP participating clinicians were similar to their specialties nationally.<sup>19</sup>

## 2. *Test Frequency*

- Interval – Recommended screening intervals for LBC differ across organizations. The USPSTF and ACOG support using the same screening intervals for conventional cytology and LBC: annual screening with screening every 2-3 years for women  $\geq 30$  years of age with 3 negative cytology tests. The ACS recommends annual screening with conventional cytology and biennial screening with LBC, both with screening every 2-3 years for women  $\geq 30$  years of age with 3 negative cytology tests (Table 1).

## 3. *Test Costs*

- Test Reimbursement Rates – The average Medicare reimbursement rate for LBC is \$26.78. This cost does not include provider fees.
- Repeat Medical Procedures/Appointments – Approximately 8 to 10 percent of LBC tests require repeat testing because of ASC-US or unsatisfactory samples.<sup>46</sup> Most of the studies that address the issue of sample adequacy are based on data collected prior to Bethesda 2001. Because the Bethesda 2001 adequacy criteria are more stringent, the rate of unsatisfactory samples may be higher as the criteria are applied. With increasing provider use of LBC and more feedback about unsatisfactory samples, these rates should decline over time. The variation in ASC-US rates using LBC likely reflects inherent inter-observer variability in gynecologic cytology.<sup>49,50</sup> Most studies find less variability with LBC compared to conventional cytology, however, this is not a uniform observation.<sup>48</sup>

Because only a portion of the LBC sample is used in preparing the slide for cytologic examination, residual material can be used for HPV DNA reflex testing for ASC-US findings. A small proportion of LBC samples, only about 5 percent, will have insufficient residual fluid to perform HPV DNA testing and will require collection of a new sample. All conventional cytology requires the collection of a separate sample at the time of the cervical swab or a return visit by the patient for collection of a new sample. The NBCCEDP provides reimbursement for reflex testing. Preservation of DNA is required for HPV DNA testing, and differing LBC fixatives and storage conditions will affect the quality of DNA. Reflex testing requires cytology labs to establish an infrastructure to assure proper retrieval of samples and to assure no sample-to-sample DNA contamination. LBC samples also may be used for immunohistochemical testing, such as p16 or

other markers that may be found to be beneficial in screening in the future. Reflex HPV DNA testing for ASC-US interpretations does include some increased costs associated with the time spent discussing test implications before it is performed and discussing positive results with patients. Quality-of-life consequences also may arise for some patients when they are told they have a sexually transmitted infection.<sup>51</sup>

#### 4. *Clinical Factors*

- Practice Patterns – Evidence suggests that more than three-quarters of those providing Pap tests, now use LBC,<sup>18</sup> and similar levels of LBC use appear among NBCCEDP participating clinicians.<sup>19</sup> As clinicians integrate LBC technology into their practices, many no longer keep supplies necessary for conventional cytology and proficiency levels in slide preparation, fixation and interpretation may decline with infrequent application.
- Clinical Efficiency – LBC holds great potential for increasing clinical efficiency over conventional cytology because samples yielding ASC-US findings can be used for HPV DNA testing, thus avoiding second office visits. However, this efficiency is offset by requirements for increased patient education about HPV and the possibility of reflex testing as well for obtaining informed consent. While no studies have specifically assessed the extent to which these offsetting requirements result in a net gain or loss of efficiency, key informant interviews and general provider impressions suggest important gains in clinical efficiency associated with use of LBC.

Clinical efficiency also is enhanced by the relative ease of microscopic interpretation of LBC-derived samples compared to conventional cytology and the resulting preference by microscopists for LBC-derived samples. It is not clear, however, that this leads to improved disease outcomes. While the proportion of all unsatisfactory cytology samples is quite low, evidence does suggest that LBC may yield more samples that are unsatisfactory for interpretation. A randomized controlled trial comparing conventional cytology and LBC in Switzerland found 1.4 percent unsatisfactory samples for LBC compared with 0 percent for conventional cytology.<sup>52</sup> Other studies have found higher rates of adequate smears with liquid based cytology.<sup>46,53,54</sup>

#### 5. *Patient Factors*

- Age – LBC is appropriate for women 3 years after the initiation of sexual intercourse or by age 21, whichever occurs first. The NBCCEDP currently screens women beginning at age 18.
- Acceptability/Adherence – Because of the similarities in exam procedures, most women find LBC at least as acceptable as conventional cytology. Patients are increasingly aware of LBC because of direct-to-consumer marketing. While LBC false-positive rates are likely higher than those of conventional cytology, some women find this an acceptable trade-off with higher test sensitivity and resulting increases in the likelihood that LBC will identify neoplasia. Potential harms that

may result from the increased sensitivity of LBC include the over treatment of CIN 1 and CIN 2. HPV reflex testing using existing LBC samples increases adherence to ASC-US follow-up, but this advantage does not extend to follow-up for other abnormal findings.

#### **6. Program Factors**

- Program Efficiency – As increasing numbers of clinicians and pathology laboratories adopt LBC larger proportions of program providers must absorb cost differentials or develop different strategies of care for NBCCEDP clients and other patients. Program staff must manage the consequences of both strategies, and this can cause considerable time in resolving billing conflicts, case management and explaining reimbursement policies to providers. Further, because of the ability to perform HPV DNA testing with LBC, program staff spend less case management time scheduling follow-up visits for ASC-US findings and fewer women are lost to follow-up.
- Provider Enrollment – As discussed above, clinical practice patterns are increasingly shifting to exclusive use of LBC. Many providers report difficulty finding pathology laboratories that accept conventional cytology tests for interpretation. Many laboratories find screening and interpretation of LBC specimens to be faster and easier than conventional cytology. Both options of either maintaining two approaches to cervical cancer screening, conventional cytology for NBCCEDP patients and LBC for other patients, or absorbing the cost difference associated with providing LBC to NBCCEDP patients and accepting conventional rate reimbursement, place burdens on program providers. The overall magnitude and impact of sustaining these burdens increases over time and can adversely affect provider recruitment.
- Continuity of Care – Continuity of care depends on women forming sustained relationships with their providers. Disincentives for provider participation in the NBCCEDP could reduce provider involvement with the program or increase the turn-over rate of participating providers. Both consequences potentially affect continuity of care for women in the program. Further, the advantages of HPV reflex testing using LBC samples may extend to tests for other STDs.

#### **Human Papillomavirus Testing**

The FDA approved use of combined HPV DNA and Pap testing for screening of women over 30 years of age in March 2003. HPV DNA testing as a single test for screening has not been identified by the FDA as being “safe” or “effective.” However, it has been shown to be both safe and effective when used in conjunction with a cytology sample for women over 30 years of age, and repeated every 3 years if both tests are negative. Combined testing can be performed with either conventional cytology or LBC.

The advantage of combined HPV and cytology testing over cytology testing alone is a small increase in the negative predictive value, allowing for safe extension of screening intervals. Sherman, et al., showed an increase in negative predictive value 45 months after baseline testing, from 99.47 for Pap alone to 99.84 for the combined tests.<sup>55</sup> The USPSTF review

found insufficient evidence to recommend for or against HPV DNA testing as a replacement for or adjunct to cytology testing. The ACS and ACOG have recommended HPV DNA as an acceptable adjunct to cervical cytology in women over age 30 years. If both cytology and HPV test are normal, retesting is not needed for 3 years.

### **1. Performance Characteristics**

- Sample Adequacy – Occasionally, insufficient material for HPV DNA testing remains after the cytologic examination if LBC is used. The proportion of limited samples tends to decrease as clinicians gain experience with efficiently dislodging cells into the collection fluid (Elizabeth Unger, personal communication).
- Sensitivity – The sensitivity of a positive Hybrid Capture 2 test for high-risk HPV types in the setting of ASC-US cytology for detecting histology proven HSIL or greater ranges from 62 to 95 percent.<sup>2, 56</sup>
- Specificity – The specificity of a positive Hybrid Capture 2 test for high-risk HPV types in the setting of ASC-US cytology for detecting histology proven HSIL or greater ranges from 41 percent to 94 percent.<sup>2, 56</sup>
- Reliability of Interpretation – Inter-laboratory comparison studies indicate good reliability, with reported kappa values of 0.79-0.89 between individual labs.<sup>57</sup>

### **2. Test Frequency**

- Interval – The ACS and ACOG have concluded that HPV DNA as an adjunct to clinical cytology for primary screening is acceptable in women over 30 years of age. If both cytology and HPV test are normal, testing should not be repeated for 3 years.

### **3. Test Costs**

- Test Reimbursement Rates – The average Medicare reimbursement rate for HPV DNA testing is \$46.52. Provider fees are not included. This cost is in addition to the cost of performing conventional cytology or LBC alone. The initial costs for combined cytology and HPV DNA testing are substantially higher than the costs for either conventional cytology or LBC alone. While there is some evidence of the cost-effectiveness of combined screening, the savings are largely based on adherence to a lengthened screening interval following negative cytology and negative HPV DNA. As reflected in Table 1, both ACOG and ACS recommend a similar lengthened screening interval for cytology alone, but only after three consecutive negative cytology exams and only among women 30 years of age or older.
- Repeat Medical Procedures/Appointments – When used in a screening setting in conjunction with cytology testing, positive HPV with negative cytology findings present a clinical challenge. Repeat testing with one or both modalities is recommended in 6 months to 1 year. Clear communication with patients about the meaning of a positive HPV result is required to accurately convey the need for follow-up without causing undue anxiety. Scant published data exist to determine

the proportion of NBCCEDP women that will fall in this category and their ultimate clinical outcomes, especially in women in older age groups.

#### 4. *Clinical Factors*

- Practice Patterns – One national survey of clinicians found that 59 percent of clinicians who reported providing Pap tests ordered HPV tests for patients with borderline or abnormal Pap results, and 21 percent reported ordering HPV tests as an adjunct to Pap testing.<sup>18</sup> Substantial industry marketing to providers and patients is increasing awareness of and demand for use of HPV tests. Because about three quarters of clinicians report using LBC, most of the HPV tests conducted as follow-up to abnormal cytology findings are performed as reflex tests without a follow-up patient visit. Follow-up of ASC-US without reflex HPV testing, on the other hand, requires a second office visit or collection of two samples at the time of initial cytology. These requirements can reduce provider resources. Provider time spent for a second patient visit is time unavailable for other program women. Co-collection of samples for conventional cytology and HPV tests requires additional supplies, unique procedures for collection, preservation, and storage of samples, physical storage space, and procedures for tracking and ensuring that there is no sample contamination.
- Clinical Efficiency – Clinical efficiency associated with use of HPV testing as a reflex test for ASC-US findings, stems from reduced patient visits (See LBC: Clinical Efficiency on page 20). The use of HPV DNA testing as an adjunct to cervical cytology can increase efficiency by removing low-risk women, those with both negative Pap and HPV results, from the pool of those needing annual screening. Among patients who test positive for HPV but have a negative cytology finding, additional patient education and associated provider time is required because of the complexity of follow-up as well as patient understanding of HPV as a sexually transmitted virus.<sup>58</sup>

#### 5. *Patient Factors*

- Age – Screening with HPV DNA as an adjunct to cervical cytology is recommended only for women over 30 years of age.<sup>1,3</sup> An upper age limit of testing is not known, though some data suggest that HPV DNA positivity rises as age progresses.
- Acceptability/Adherence – HPV DNA testing as an adjunct to screening cytology can extend the screening interval among women older than 30 years of age when both tests are negative and without requiring 3 consecutive negative exams. Although longer time between screening exams might make HPV testing more acceptable to some women, others might become anxious with less frequent screening. Some patients prefer to be tested every year rather than every 3 years.

Another factor that could lower the acceptability of and adherence to cervical cancer screening that includes HPV testing is that women may not want to learn that they have a sexually transmitted infection. This could result in decreased adherence compared to use of repeat cytology, which in turn can lead to

unanticipated outcomes such as an increase in overall disease prevalence.<sup>59</sup> Additional patient education would be required to explain the risk factors for cervical cancer and the benefits of regular screening including HPV DNA testing.

## 6. *Program Factors*

- Program Efficiency – The NBCCEDP already allows reimbursement for high-risk HPV DNA testing as follow-up for an ASC-US Pap result. Thus, programs have already established agreements with laboratories for processing HPV DNA testing and have already resolved many of the billing and associated start-up issues that often results from reimbursement of a new procedure. However, reimbursement for HPV DNA testing as a screening test in combination with cytology would require changes to eligibility policies, data collection and reimbursement systems, as well as case management policies. These changes would require a large amount of time and effort on the part of NBCCEDP grantees and would require much work and guidance from CDC staff. These program requirements could be further complicated by HPV DNA test consent requirements that would allow women to decline combined testing. To accommodate these cases, program procedures would need to be established to handle cytology either alone or in combination with HPV DNA testing.

Program efficiency resulting from combined cytology and HPV testing could result from longer recommended screening intervals among women for whom both tests are negative, screening no more frequently than every 3 years. Program savings could result from less case management time, billing and financial processing, as well as monitoring and tracking on a per patient basis. However, there is little experience to show whether patients and providers will adhere to lengthened screening intervals. For other cancer screening exams with intervals longer than 1 year, such as colonoscopy and cervical cytology following 3 consecutive negative exams, there is some evidence to suggest that repeat exams are performed in intervals that are shorter than recommended.<sup>60</sup> If a large enough proportion of NBCCEDP women return for and receive repeat screening sooner than 3 years, net increases in program costs could be seen. This could result in a greater likelihood of false-positive screenings and unnecessary and costly diagnostics. The transient nature of the population served in the NBCCEDP makes tracking of prior screening histories challenging for programs and providers. Finally, because of the clinical challenges associated with discordant findings on the two tests, particularly, negative cytology and positive HPV testing, combined screening could increase the amount of case management time required and associated costs in the program.

- Provider Enrollment – Only about 21 percent of providers in the NBCCEDP currently order HPV in combination with cytology.<sup>18</sup> Lack of NBCCEDP reimbursement for HPV DNA testing combined with cytology does not seem to be having the same impact on provider enrollment.
- Continuity of Care – It is unclear whether there is any relative change in the continuity of care for women who receive combined cervical cytology and HPV



DNA testing compared with conventional or LBC cytology alone. It is possible that lengthening future screening intervals for women with combined normal results could have a detrimental impact on adherence with schedules for regular care, including annual mammograms, clinical breast exams, or other screenings such as for high blood pressure. On the other hand, HPV testing provides a unique opportunity for STD counseling.

## **POLICY RECOMMENDATIONS**

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Following careful review of the test characteristics and public health factors associated with each technology, the NBCCEDP Cervical Cancer Expert Panel discussed potential reimbursement policies and the supporting rationale for each option. Panel members reached consensus on specific recommendations for reimbursement policies and identified the key factors providing the rationale for their recommendation. These recommendations and rationale for each are presented below.

### **Conventional Cytology**

#### Reimbursement Policy Recommendation

Continue reimbursement for annual screening with conventional cytology (Pap testing) and screening every 2-3 years for women  $\geq 30$  with 3 negative cytology tests.

#### Rationale

- No new evidence has emerged to warrant a change in existing policy.
- Morbidity and mortality from cervical cancer have declined substantially since the introduction of conventional cytology.
- Conventional cytology is well integrated into existing clinical practice.
- Conventional cytology is well accepted among patients.

### **Liquid Based Cytology (LBC)**

#### Reimbursement Policy Recommendation

Allow reimbursement for biennial screening with LBC.

#### Rationale

- Patient acceptability of LBC is high due to test administration similarities with conventional cytology.
- No additional provider time or training is required for performing LBC, making clinical efficiency for LBC high. While some additional supplies might be required, these should be covered under Medicare reimbursement rates.
- Ease of HPV triage for ASC-US interpretations enhances both clinical efficiency and patient acceptability/adherence, because requirements for repeat patient visits are reduced. These advantages are weighed against patient and program costs associated with likely overall increased cytology positivity rates, especially for LSIL interpretations. Higher false-positive rates are in part an artifact of interpreter inexperience with the new technology, and trends suggest the levels of false-positive findings are declining with increasing experience. HPV triage of ASC-US interpretations, however, can assist in distinguishing between false-

positive and potentially true-positive findings. Despite these trends, however, increased rates of false-positive findings result in downstream program costs for follow-up tests and case management as well as patient burdens associated with unnecessary follow-up.

## **HPV DNA Testing**

### Reimbursement Policy Recommendation

Reimbursement for combined cytology and HPV testing among normal, asymptomatic women is not recommended at this time. Reimbursement for HPV testing as an option for follow-up of ASC-US cytology is recommended. HPV testing recommendations should be reviewed in one year to consider findings soon to be published from general population screening studies assessing cytology and HPV testing in a large health maintenance organization.

### Rationale

- Insufficient evidence exists to support HPV DNA testing as an alternative or adjunct to cervical cytology screening. Although HPV DNA testing may have a future role in distinguishing between women who would benefit from annual testing and those for whom extended screening intervals or even discontinued screening may be appropriate, current evidence is insufficient to support combined testing at this time. Ongoing randomized trials on HPV testing should provide additional evidence on these issues over the next several years.
- Use of HPV DNA testing as an alternative or adjunct to screening cytology trades off testing for higher prevalence HPV versus lower prevalence abnormal cytology. The morbidity and mortality consequences of this trade-off are unknown. Further, such a trade-off could result in higher follow-up rates and associated program and patient costs. Published data are lacking to determine prevalence rates of high-risk HPV DNA positivity in women similar to those served by the BCCEDP and persistence of HPV DNA positivity in women who are found to be high-risk HPV positive but have a normal cytology test.
- Considerable patient and provider education would be required concerning the epidemiology of high-risk HPV, its relationship to cervical cancer, and the benefits and shortcomings of HPV testing.
- While provider and direct-to-consumer marketing may increase demand for HPV testing as an alternative or adjunct to cervical cytology, current levels of market penetration appear to be low.

## **Other Recommendations:**

### **Research & Surveillance**

- Implement demonstration projects to assess the cost/benefit and implementation challenges of biennial LBC.
- Conduct studies to assess patient and provider perceptions and behavior related to extended screening intervals (e.g., 2 years, 3 years) and strategies for increasing acceptability of longer intervals.
- Gather NBCCEDP surveillance data about actual provider and laboratory practices in the use of LBC and other technologies.

- Assess the extent of clinical practice adherence to screening guidelines (e.g., intervals, age, etc.), reasons for deviations, and practice differences between NBCCEDP and non-program patients.
- Implement demonstration projects to assess the benefits, harms and acceptability of including HPV DNA testing as an adjunct to primary cervical cytology screening using various cytology platforms.

#### **Education**

- Working with ACS and ACOG, implement public and provider education to increase understanding of the potential harms of low test specificity/high false-positive rates and the relationship of test intervals to test and disease characteristics.

#### **Reimbursement Policy Review Process**

- The CDC should assess whether new technologies and/or data have emerged that could change current reimbursement policies on an annual basis. In the presence of new technologies and/or data that may influence policy decisions, an expert panel review of policies should be undertaken. A full policy review should be undertaken at least every 5 years. USPSTF evidence reviews should be utilized to prevent duplication of effort.

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## APPENDIX A: KEY INFORMANT INTERVIEWS

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### EVALUATION OF NBCCEDP REIMBURSEMENT POLICIES FOR NEW BREAST AND CERVICAL CANCER SCREENING TECHNOLOGIES

#### INTRODUCTION

The National Breast and Cervical Cancer Early Detection Program (NBCCEDP), administered by the Centers for Disease Control and Prevention (CDC), helps low income, uninsured, and underserved women gain access to lifesaving screening programs for the early detection of breast and cervical cancers. The program implements a wide range of activities, including a) public education and outreach to increase access to services; b) administration of breast and cervical cancer screening exams and diagnostic testing; c) case management to facilitate access to care and utilization of best practices; and d) professional education and quality assurance to ensure the highest standard of care for women in the program. The NBCCEDP is implemented in all 50 states, 4 U.S. territories, the District of Columbia, and 13 American Indian/Alaska Native organizations. While the program has screened 1.9 million women and provided 4.6 million screening examinations since its inception in 1991, it reaches fewer than 20 percent of eligible women, primarily due to financial limitations.

While the size and complexity of the NBCCEDP poses many challenges, one challenge has been the determination of which screening and diagnostic tests should be paid for by the program. Since the programs inception, scientific advances have resulted not only in improvements to existing screening and diagnostic tests and implementation procedures, but also in the introduction of new technologies. Determinations about whether the NBCCEDP should pay for use of newer screening and diagnostic tests and procedures are complicated. The program must balance a wide range of factors, including for example, standard of care for women in the program, the public health mandate to serve as many women as possible, limited program funds, varying local health services infrastructures, and the impact of changes in program policies on program operating procedures and partners.

The CDC is reviewing the NBCCEDP reimbursement policies for breast and cervical cancer screening and diagnostic services. For breast cancer, the NBCCEDP currently provides reimbursement for film mammography only. Digital mammography, magnetic resonance imaging (MRI), and ultrasound are not reimbursed as screening tests. Computer aided detection (CAD) of digital mammograms is not reimbursed. For cervical cancer, the NBCCEDP provides reimbursement for conventional pap tests, but not for liquid-based pap tests. HPV/DNA testing is reimbursed only for women with ASC-US findings on pap.

Recognizing the complexity of this task and the significant impact on individual BCCEDP programs, the CDC sought to gather additional information about programs' experiences with reimbursement policies. Key informant interviews with NBCCEDP program directors representing eight state programs and two CDC program staff were conducted to gather information about the range of issues that should be considered in CDC's evaluation of its reimbursement policies. Specifically, interviews sought to provide information about:

- a) The type and magnitude of NBCCEDP challenges resulting from current reimbursement policies for screening technologies;



- b) NBCCEDP approaches for addressing challenges associated with current reimbursement policies;
- c) The range and nature of NBCCEDP modifications that would need to be made to adjust to potential modifications of current reimbursement policies for new screening technologies; and
- d) How appropriate balance might be achieved across scientific, infrastructure, programmatic, and public health impact factors in decision-making concerning NBCCEDP reimbursement policies.

## **METHODS**

Interviews were conducted in December, 2004 with NBCCEDP program directors representing eight state programs and two CDC program staff. NBCCEDP program directors volunteered to participate in key informant interviews following an invitation from the NBCCEDP Science and Epidemiology Subcommittee. Program Directors could include other program staff in interviews at their discretion.

Email interview confirmations included an overview of the key informant assessment and a list of questions to be addressed in each interview. Four of the eight interviews with NBCCEDP program directors focused on breast cancer and the remaining four focused on cervical cancer. Interviewees were not restricted, however, from identifying issues beyond the specific cancer focus for their interview and most interviewees addressed reimbursement issues related to both cancers. Each interview was conducted by telephone by Dr. Marianne H. Alciati. Interviews lasted between 45 and 75 minutes. Handwritten interview notes were taken during each interview and a typed summary was prepared following each interview. These summaries were used as the primary information source for analysis. Interviews were tape recorded for verification purposes only and all tapes were destroyed at the end of the analysis.

Each interview summary was reviewed to identify themes and representative issues. Because the purpose of this assessment was to identify the range and nature of reimbursement challenges faced by the NBCCEDP and the sample size was so small, the specific numbers of mentions for each issue and the number of interviewees mentioning each issue was not calculated. However, general comments are presented reflecting whether a particular issue was identified by multiple sites.

## **LIMITATIONS**

It is important to recognize that while the data from these interviews provides a valid picture of issues across the eight programs and from the perspectives of two CDC staff, it does not provide information about the pervasiveness of these issues across NBCCEDP sites and only generally provides perspective on the magnitude of each issue within NBCCEDP programs. While it is generally accurate that the eight programs combined with CDC staff perspectives are typical of NBCCEDP programs, the diversity across NBCCEDP programs and the method for selecting key informant interviewees suggests that the experiences of these programs may not be representative of all programs. It is possible and even likely, that some additional issues or examples exist within other programs. However, these interviews do provide a clear and accurate picture of the majority of issues resulting from current reimbursement policies and changes in policy.

## RESULTS

NBCCEDP programs are complex local partnerships, involving extensive networks of providers and health care organizations who deliver screening and diagnostic examinations and help provide and coordinate follow-up care. Reimbursement for screening and diagnostic services is at the heart of the program, representing a significant driving force for how the NBCCEDP programs operate within local communities. Reimbursement policies influence not only what services these programs provide, but also how efficiently they provide those services and how the programs are perceived within their local communities and nationally.

Interviewees identified a broad range of issues associated with existing reimbursement policies as well as historic and current procedures for modifying these policies and communicating revisions. The vast majority of these issues were similar for both breast and cervical cancer reimbursement policies. For this reason, this presentation of results focuses on these issues and their common characteristics with illustrative examples from breast and cervical cancer. While most of the interview results focus on factors that influence demand for new technologies and the challenges posed by current reimbursement policies and review procedures, two significant overriding perspectives were emphasized by the majority of interviewees. First, the NBCCEDP provides a critical public health service and program participants are extremely committed to the NBCCEDP's success. Second, interviewees were extremely appreciative of the opportunity to provide input to the policy review process and of the CDC's commitment to and efforts on behalf of the NBCCEDP.

All NBCCEDP programs are required to reimburse at rates that do not exceed state Medicare rates. Although different state formulas may be used to establish these rates (e.g., urban vs. rural rates), they are quite low and in some cases below the actual cost of delivering the service. Several interviewees pointed out that some costs associated with providing diagnostic and follow-up procedures to this population are not reimbursable using CDC funds. These costs are often paid by state funds (not available in all states), grants, donations, or other sources; or absorbed by the facility or provider. But both of these options add pressure to the system of delivering NBCCEDP services. Newer technologies further exacerbate this pressure because they are often more expensive, although costs tend to decline over time. The consequence of higher costs for individual screening and diagnostic exams is a reduction in the programs' overall capacity to "achieve the greatest good for the greatest number." The reality that the program currently reaches only 20 percent of the eligible target population makes these trade-offs particularly difficult.

***Program Consequences:*** But as revealed in these interviews, the issues go well beyond simple cost calculations. A broad range of consequences result from NBCCEDP reimbursement policies. These are presented below in five broad categories, including a) program performance, b) relationship with providers, c) practice patterns, d) standards of care, and e) program credibility.

***Program Performance:*** Interviewees emphasized that the cost to individual programs of different reimbursement policy decisions have affects well beyond just the cost of individual examinations. In some areas, the failure to reimburse newer technologies has reduced the number of providers who deliver services for the program causing program shortages. In other

cases, providers have used their size or banded together with other providers to pressure the program to reimburse for newer technologies at the approved Medicare rates.

Reduced provider capacity can limit both the programs' ability to meet demand for early detection services as well as cause delays in providing needed services. Delays, in turn impact Minimal Data Element (MDE) reporting and a program's ability to achieve service delivery targets. Examples were noted in NBCCEDP's failure to reimburse for liquid-based pap (LBP) examinations. The paucity of providers performing conventional pap in some areas required women to travel for services, resulting in screening delays or failures to get screening.

Another impact of reimbursement policies on program performance relates to efficiency. In cases of an abnormal pap, use of conventional pap rather than LBP requires a second office visit and additional call-back efforts. This process was noted both to increase the likelihood that follow-up HPV testing would not be accomplished and to drain limited resources due to the need to find women and to pay for a second office visit. Other inefficiencies emerge as well. The need for alternate funding to cover costs for un-reimbursed services takes time and resources, not only to identify sources of funds, but to establish systems that account for separate sources of funding.

Beyond complications associated with existing policies, changes in reimbursement policies have extraordinary implications for program operations. Providers and their staff need to be made aware of new policies, corresponding CPT codes need to be identified and populated in reimbursement systems, data and reporting systems need to be modified, and contract requirements need to be adjusted. Ideally, program policy manuals also would be updated. Some programs indicated that listings of reimbursed procedures are not included in their program manuals because of the unpredictability of policy changes and, in at least one case, the reversal of a policy within a six month timeframe. Failures to include reimbursement information in policy manuals introduces another set of operational requirements, such as development of a separate listing of reimbursable services and increased communication to clarify reimbursement policies and procedures with providers and their staff.

*Relationship with Providers:* Many interviewees discussed the pressures on providers and their relationship with the program resulting not only from low reimbursement rates, but from a complex interplay of other factors. Providers historically have born much of the responsibility for ensuring follow-up and treatment for women diagnosed through the program. For breast cancer in particular, medical liability risks are high. Failure to diagnose breast cancer is the primary cause in the U.S. for malpractice claims and the second-leading reason for subsequent claimant payments. Providers also are challenged to keep pace with complex scientific evidence and medical advances. Media publicity further complicates this challenge as patients request and sometimes demand newer technologies that may not be reimbursable through the program. These factors are compounded when newer technologies become available in the market but are not reimbursed by the program and when the NBCCEDP changes what services can be reimbursed under the program.

Many interviewees commented on the extra financial burden to providers when they must absorb the additional cost difference between BCCEDP approved technologies and newer technologies. While most interviewees commented on the high level of commitment of providers to the NBCCEDP, this added burden is perceived to strain that commitment. In some areas providers

have left the program, but more often interviewees indicated that under current policies, providers remain with the program in hopes of upcoming policy changes.

Other consequences for providers were noted, particularly in the ethical dilemma of delivering what, in some cases providers believe to be less than the best care available. In this way, reimbursement policies are viewed as driving the practice of medicine, changing the role of the provider, and changing the patient/provider relationship. Providers in these situations are “pressured” to offer only covered services. In this role, as one interviewee commented, the program is not a “legitimate partner.” Further, many women will not get services until they are assured that they will not be billed. This tension is compounded when patients learn about new technologies through the media, advocacy organizations, or other sources and question the care they receive through the program. Differential treatment as noted by some interviewees fuels distrust between patients and providers.

Reimbursement policies that do not include newer technologies, particularly when they are available within a provider’s health care setting, also increase liability risks. Failure to provide a test or procedure in situations where a cancer is later identified increases the providers’ vulnerability to litigation, particularly if the decision appears based on cost.

All these factors combine to define the relationship between the programs and providers. All interviewees commented on the importance of building and maintaining strong relationships with the providers in their program. Several noted that reimbursement issues have created tension, most notably reflected in ‘uncomfortable’ dialogues in which program staff find themselves ‘arguing with providers’ about interpretations of scientific evidence, or countering a provider’s direct experience with a technology (e.g., LBP is easier to read). Interviewees noted that they expend a lot of time and effort communicating with their providers about the science and rationale behind current reimbursement policies. Some position these policy communications as the program staff and providers on one side and CDC on the other. Often program staff appears to be ‘stretching’ the commitment of providers until policies change in time.

*Practice Patterns:* It became clear across interviews that different localities adopt newer technologies at different rates. For example, in some areas labs have gone exclusively to LBPs or CAD. In cases where only the newer technology is available, newer technologies are reimbursed at the rates of approved technologies. But newer technologies are often more expensive and the added cost difference must either be absorbed by providers or reimbursed through alternative funds, placing added strain on providers and alternate sources of funds. Several interviewees noted that procedures for providing and billing for new technologies at the rates of approved technologies preclude analysis of the frequency of this practice within the program.

Incompatibilities with existing local health care practices also can lead to inefficiencies and open the door for error. In some cases, the cost difference has been billed directly to women participating in the program. For example, a few interviewees conveyed stories of the cost difference between film mammography and digital mammography with CAD or between conventional pap and LBP, estimated at about \$60 in each case, being billed directly to women. In some instances, these cases have gone into collections, placing extraordinary and unnecessary burden on women in the program. If an abnormality is identified, some providers back-bill this

cost difference to Medicaid. While direct billing to women is disallowed by the program and the situations identified were ultimately resolved, they require considerable staff time and resource as each case must be addressed individually. These situations also extol a price in terms of women's negative experience with the program.

Another example provided by several interviewees of NBCCEDP reimbursed practices being out of step with local practices was the approval for cervical cancer testing using the Digene system. This process allows two samples to be captured during an initial patient visit, one for conventional pap and a second for HPV testing following an abnormal pap. But in most facilities, this procedure applied only to NBCCEDP clients and facilities did not have the capacity to properly store the second sample for potential follow-up. In many cases facilities were unfamiliar with the system altogether.

Another concern stemming from continued use of approved technologies for NBCCEDP women when facilities and providers have transitioned to newer technologies is perceived decline in proficiency by providers for technologies that they no longer perform with the same frequency. For example, one interviewee noted provider concerns about their proficiency interpreting pap slides due to declining frequency associated with increased use of LBP.

*Standards of Care:* As noted above, providers raise concerns about providing care through the NBCCEDP that is "less than optimal care." But these concerns appear to extend well beyond providers and in reality are fueled both by media coverage and public promotion of medical advances and pharmaceutical marketing efforts directed to providers that may oversell the science behind new technologies. Interviewees raised concerns about both the reality and perception that women in the NBCCEDP receive a different standard of care than those with the financial means to pay for health care. Several interviewees spoke of an emerging, two-tiered system of health care where the poor receive a lower level of care. This raised both public health and ethical concerns.

*Program Credibility:* Perceptions of a different standard of care for women in the NBCCEDP was viewed as one of several factors that undermine the credibility and reputation of the program. But several interviewees also noted that inefficiencies resulting from reimbursement policies that differ from common practice, as discussed above, also undermine the program's reputation. Resentment was reflected in one local program where providers 'banned together' to demand reimbursement at Medicare rates for LBP. Bad will is also generated when women are billed for differential costs, as in the cases noted above for LBP and CAD.

Perceptions that the NBCCEDP is 'out of step' with current technology has other ramifications as well. One program conveyed an interesting scenario in which their program was unable to participate in a collaborative research study with academia and the Indian Health Service to assess the impact of digital mammography on access to care for underserved, rural populations. The study was viewed as having great potential for expanding the program's reach, but the program's inability to participate because digital mammograms could not be reimbursed was viewed as reducing program credibility. In this case and more broadly in the program provider relationship, some interviewees indicated these situations threatened the viability of the program as a credible partner in meeting the needs of underserved women.

Finally, several interviewees commented on discrepancies between the reimbursement policies of the NBCCEDP and policies of other federal programs, such as reimbursement by Medicare and approvals for use of new technologies by the Food and Drug Administration. These inconsistencies are confusing and increase the challenge and importance of program communications. Several interviewees also perceived these discrepancies as reducing NBCCEDP credibility.

**Review Procedures:** The majority of interviewees commented on the historic and current process for revising reimbursement policies. Most expressed appreciation for the interview process and CDC's efforts to include their perspective in the current review of these policies. Continued involvement of multiple perspectives, and particularly NBCCEDP Program Directors was viewed very favorably. Many positive changes were noted in reimbursement policies over the past several years, in particular approvals for loop electrode excision and cold-knife conization of the cervix as diagnostic procedures and HPV testing as follow-up to ASC-US results on pap. Many also noted the improvements resulting from legislative action in 2001 to allow treatment reimbursement through Medicaid.

But the rare instances where policy changes had been made and reversed stood out. Reversals were perceived as program ineffectiveness and "taking something away." This situation required considerable staff time and resources to revise systems and communicate with program partners, and resulted in large credibility costs. In the context of policy revisions, interviewees again emphasized the large ripple effect of changes, requiring changes in recruitment and outreach, data and coding systems for reimbursement, provider education, and MDE reporting.

Several interviewees also commented specifically on the timing of policy revisions. These reviews are not conducted on a fixed schedule and announcements about revisions are not coordinated with impacted program cycles, such as contract renewal dates.

Systems for communicating policy revisions do not appear to be reaching all programs equally. Several interviewees emphasized the importance of enhancing communication about reimbursement policies as well as the process and rationale for policies, both between CDC and the programs, and between program staff and providers. Standardization of the process was often advocated, however, interviewees varied in their perspectives about how flexible final policies should be. Some saw value in flexibility, allowing the individual programs to adjust to local circumstances such as different practice patterns and rates of adoption of new technologies. Others advocated for "hard and fast rules" that they perceived to alleviate confusion shift the burden of unpopular reimbursement decisions to CDC rather than the local program. Some interviewees highlighted the importance of CDC support and assistance translating reimbursement policies into implementation procedures, such as aligning CPT codes to reimbursable procedures.

Finally, across interviewees a number of criteria for reimbursement policy determinations were identified. These included:

- Impact – ensure that policies extend the reach of the NBCCEDP.
- Scientific credibility – policies must be evidence-based, reflecting support for the most effective technologies.

- Cost-benefit – cost benefit analyses that account for all program costs – exam/procedure costs, implementation costs, and credibility costs – must support the overall benefit of new technologies.
- Current and future practice patterns – analysis of the rate of adoption of new technologies and the consequences of different program procedures must be considered.
- Consistency – policies should seek to minimize inconsistencies across national guidelines and federal programs that can adversely affect implementation.

## CONCLUSIONS

The NBCCEDP is clearly a critical and valued public health program seeking to meet a need well beyond its resources. CDC, program staff, providers and many other key program partners demonstrate extraordinary commitment to the goals and implementation of the program. But the program is complex, with a broad array of factors influencing its capacity to maximize the delivery of services. Reimbursement policies for program services are at the apex of this web of influences. The key informant interviews conducted for this assessment identified and organized these influencing factors as a basis for more fully and systematically considering the impact of different reimbursement policies on the NBCCEDP. The primary factors identified include program performance, the program's relationship with providers, practice patterns, standards of care, and program credibility.

These interviews also identified strategies for improving the review and implementation process for reimbursement policy revisions, including a) involving multiple perspective, particularly at the program level, b) establishing a standardized process, and c) coordinating the timing of revisions with program cycles impacted by policy revisions. Clear criteria that consider program impact, scientific evidence, cost/benefit, practice patterns and continuity should be applied. And stronger systems must be established for communicating policy decisions and their rational throughout the many partners of the NBCCEDP.

## APPENDIX B: EXPERT PANEL MEMBERS

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1) Digene Corporation manufactures and sells an FDA approved HPV DNA test for use with cytology screening for cervical cancer. As Vice President, Women's Health at Digene Corporation, Dr. Alexander is responsible for public and provider education about HPV and cytology screening. Dr. Alexander abstained from all panel votes concerning recommendations for reimbursement of HPV testing.

2) Director, State Breast and Cervical Cancer Early Detection Program

3) Member, Breast and Cervical Cancer Early Detection and Control Advisory Committee